

JP 01-135,711

JP 01-135711

**Best Available Copy**

---

Translated from Japanese by the Ralph McElroy Translation Company  
910 West Avenue, Austin, Texas 78701 USA

Code: 5000-77497

JAPANESE PATENT OFFICE  
PATENT JOURNAL (A)  
KOKAI PATENT APPLICATION NO. HEI 1[1989]-135711

Int. Cl. <sup>4</sup> :	A 61 K 7/06
Sequence Nos. for Office Use:	7430-4C
Filing No.:	Sho 62[1987]-294005
Filing Date:	November 24, 1987
Publication Date:	May 29, 1989
No. of Inventions:	1 (Total of 4 pages)
Examination Request:	Not filed

HAIR GROWTH PROMOTING AGENT

Inventors:	Tadayoshi Miyashita Kobayashi Kosei Research Laboratory 48-18 Sakae-machi, Kita-ku, Tokyo
	Chiharu Watanabe Kobayashi Kosei Research Laboratory 48-18 Sakae-machi, Kita-ku, Tokyo
	Minoru Takahashi Kobayashi Kosei Research Laboratory 48-18 Sakae-machi, Kita-ku, Tokyo
Applicant:	Kobayashi Kosei K.K. 3-6-2 Nihombashi, Chuo-ku, Tokyo

[There are no amendments to this patent.]

### Claim

1. A hair growth promoting agent, characterized by being a blend of one or more effective components selected from pulegone, piperitenone, isopiperitenone, carvenone, cycloshipenone [transliteration], diosphenol and karahanaenone and essential oils containing these substances as primary components.

### Detailed explanation of the invention

#### Industrial application field

This invention pertains to a novel hair growth promoting agent incorporating specific substances having an  $\alpha,\beta$ -unsaturated keto structure or essential oils containing said substances as the main active components, and more specifically, it is to provide a hair growth promoting agent having excellent hair growth promoting and nourishing effect for stimulating or normalizing hair and scalp functions.

#### Prior art

Conventionally, various hair growth promoting agents have been utilized for preventing and treating various physiological symptoms including alopecia, thinning hair, dandruff and seborrhea.

In general, the purpose of using drugs incorporated in a hair growth material, a so-called hair growth promoting agent, lies mainly in stimulating the blood circulation in the scalp, activating the trichocytes, suppressing sebaceous secretion from the scalp and supplying nutrients to hair, and for example, various components including vasodilators such as vitamin E and the derivatives thereof, carpronium chloride, swertianogen (swertia extract) and rheisogen [transliteration], female hormones such as estradiol and ethynylestradiol, skin function stimulators such as pantothenic acid and derivatives thereof, cepharanthine and mononitroguaiacol, keratin solubilizers such as salicylic acid, resorcinol and benzalkonium chloride, antibacterial agents, anti-inflammatory agents such as glycyrrhetic acid and allantoin, vitamins such as vitamin B6, and amino acids such as methionine and serine have been utilized for such purposes. By topically applying hair growth promoting materials incorporating these substances, dandruff and itchiness are controlled and hair loss is prevented or suppressed, and furthermore, they are expected to demonstrate hair growth and nourishing effects.

Also, in recent years, it has been said that excessive or unbalanced male hormone is the cause for hair loss, and incorporation of an antiandrogen agent in hair growth promoting agents has been investigated. Particularly, it has been suggested that  $5\alpha$ -dihydrotestosterone is involved in male alopecia as an active hormone, and there are studies aimed at suppressing its production. In other words, it is known that  $5\alpha$ -dihydrotestosterone is formed from the reduction of

testosterone by testosterone-5 $\alpha$ -reductase in the hair follicle, and therefore, it is surmised that the occurrence of male alopecia can be prevented or suppressed if the activity of testosterone-5 $\alpha$ -reductase could be hindered. For that purpose, antagonists for hindering testosterone-5 $\alpha$ -reductase activity have been investigated, and as the result, substances such as spiro lactone and progesterone were discovered as anti-androgen agents and reported to be effective as hair growth promoting agents.

Problems to be solved by the invention

In addition to having effects of hair growth and hair generation, preventing hair loss, suppressing sebaceous secretion, as well as being effective against dandruff and itchiness, a hair growth promoting agent is also expected to have high safety showing no side effects or skin irritation for long-term application.

However, although the conventional hair growth promoting agents in general are useful for preventing hair loss and improving scalp condition, there is the drawback that very few of them demonstrate the kind of hair growth promoting and hair nourishing effects that satisfies the general expectations of aggressive stimulation of hair growth and hair nourishing.

Furthermore, it has been reported that there is only a very limited effect as a hair growth promoting agent for the aforementioned substances such as progesterone, and some hormonal effect is observed. Additionally, there are also some concerns about the more or less hormonal effects of other testosterone-5 $\alpha$ -reductase-hindering steroid compounds, making them not totally satisfactory substances regarding this aspect.

Means to solve the problems

The present inventors focused on the aforementioned aspects and conducted various investigations aimed at obtaining a hair growth promoting agent having better hair growth promoting and hair nourishing effects and high safety without adverse effects such as hormonal effects. As a result, it was discovered that certain substances having a specific  $\alpha,\beta$ -unsaturated keto structure or essential oils containing such substances showed excellent hair growth and hair nourishing promoting effects and are extremely effective as hair growth promoting agents, while having very good safety. Hence, the present invention is achieved based on the discovery.

In other words, the present invention pertains to a hair growth promoting agent characterized by incorporating one or more components selected from pulegone, piperitenone, isopiperitenone, carvenone, cycloshipenone, diosphenol and karahanaenone and essential oils containing these substances as the primary components.

The constitution of the present invention is explained in the following.

In the present invention, the required substances pulegone, piperitenone, isopiperitenone, carvenone, cycloshopenone, diosphenol and karahanaenone are compounds having an  $\alpha,\beta$ -unsaturated keto structure. These compounds can be obtained from synthesis or by isolation from essential oils extracted and purified from natural plants. Essential oils containing the aforementioned substances as the main components can also be suitably utilized. For example, pennyroyal oil, mountain mint oil and American wild peppermint oil containing 65-95% pulegone, and megusa [transliteration] peppermint oil containing 30% piperitenone and 65% pulegone may be cited as the particularly preferred essential oils. In the present invention, one or more than one of these substances having a specific  $\alpha,\beta$ -unsaturated keto structure or the essential oils containing them may be selected, and combined if necessary, and incorporated.

The amount of incorporation is important in terms of utilizing an effective amount of the aforementioned substances sufficient to achieve the desired purpose, but there are no limitations. However, taking into consideration the product appearance and odor, the substances are incorporated in the range of 0.001-5.0 wt%, and preferably at 0.1-3.0 wt%, based on the hair growth base materials.

Accordingly, through the application of the aforementioned substances or essential oils to the scalp and hair, hair growth promoting and hair nourishing effects can be realized by the stimulation or normalization of the functions of the scalp and hair. Furthermore, the aforementioned specific substances and essential oils have been confirmed to have high safety without any skin irritation based on human patch tests and animal testing by repeated topical application to rabbits.

Also, the hair growth promoting agent of the present invention can be applied after formulation by normal methods with known base materials of various forms generally used in hair products. As specific examples of such materials, hair tonic, hair liquid, hair lotion, hair cream, hair rinse, hair shampoo, hair setting lotion, hair spray and hair packs may be cited.

As the components for these base materials, components generally utilized in cosmetics including purified water, alcohols, polyols, oily substances such as mineral oil, oils and fats, and higher fatty materials, surfactants, skin-beautifying components, UV absorbers, viscosity agents, colorants, preservatives and fragrances may be suitably selected and used.

Moreover, in the present invention, in addition to the aforementioned required components, other generally known hair growth ingredients such as vasodilators, female hormones, skin function stimulating agents, local stimulators, keratin solubilizing agents, anti-inflammatory agents, antibacterial agents, vitamins, amino acids, herb extracts and moisturizing agents may be optionally combined and utilized, if necessary, without hindering the expectation of further improving the hair growth and nourishing effect.

### Application examples

The present invention is further explained by using application examples, however, they are not to be construed as limiting the present invention whatsoever.

### Application Example (1)

In order to confirm the effect of the present invention, tests of hair growth promoting and hair nourishing effects were conducted and investigated after the samples were prepared as shown below.

### Sample preparation

Samples were prepared by adding each test substance at the concentrations shown in Table 1 to a 60 wt% aqueous ethanol solution. The concentration of the addition is wt%.

Table 1

		① 検 体	
試 料	(11)	プ レ ゴ ン ③	1.0 %
"	(12)	ピ ペ リ タ ノ ン ④	1.0 %
"	(13)	イ ソ ピ ペ リ タ ノ ン ⑤	1.0 %
"	(14)	カ ル ベ ノ ン ⑥	1.0 %
"	(15)	シ ク ロ シ ベ ノ ン ⑦	1.0 %
"	(16)	デ ィ オ ス フ ェ ノ ール ⑧	1.0 %
"	(17)	カ ラ ハ ナ エ ノ ン ⑨	1.0 %
"	(18)	ペ ニ ー ロ ー ヤ ル オ イ ル ⑩	1.0 %
"	(19)	② プ レ ゴ ン (0.7) + ⑤ イ ソ ピ ペ リ タ ノ ン (0.3)	1.0 %
"	(20)	④ ピ ペ リ タ ノ ン 80 重量 % 水 溶 液	

- Key:
- 1 Test substance
  - 2 Sample
  - 3 Pulegone
  - 4 Piperitenone
  - 5 Isopiperitenone
  - 6 Carvenone
  - 7 Cycloshipenone
  - 8 Diosphenol
  - 9 Karahanaenone
  - 10 Pennyroyal oil
  - 11 60 wt% Aqueous ethanol solution

### Test of hair growth promoting and hair nourishing effects

Male Hartley guinea pigs with body weight of about 400 g were used. The hair on the back was removed from each of 7 guinea pigs in a group. The right side was used as the control without application and the left side was used as the test site, and 0.1 mL of each of the samples (1)-(10) was applied twice daily for 22 days. Random body hairs on the application site and the nonapplication site were removed, and the effects on the growth of the body hair of guinea pigs were investigated by determining the growth rate by measuring the length of the body hairs on the control side and the test side and determining the difference in the mean hair length of 10 hairs.

Table 2 shows the results.

Table 2

	①平均长度 (mm)	b / a	②判定
试③ (1)	1.73	6 / 7	有④效
" (2)	1.79	7 / 7	"
" (3)	1.75	6 / 7	"
" (4)	1.74	6 / 7	"
" (5)	1.86	4 / 7	有⑤效
" (6)	1.69	5 / 7	"
" (7)	1.66	4 / 7	"
" (8)	1.79	6 / 7	有④效
" (9)	1.73	6 / 7	"
" (10)	0.06	2 / 7	无⑥效

- Key: 1 Mean length  
 2 Evaluation  
 3 Sample  
 4 Significantly effective  
 5 Effective  
 6 Ineffective

$$\text{① 平均长度} = \left( \frac{\sum \text{试侧体毛} \text{②}}{\sum \text{对照侧体毛} \text{③}} \right) \times 1/1$$

- Key: 1 Mean length  
 2 Body hair on test side  
 3 Body hair on control side

$$b / a = \frac{\text{試料側の毛長の方が長い動物数} \textcircled{1}}{\text{全動物数} \textcircled{2}}$$

Key: 1      Number of animals having longer hair on the sample side  
 2      Total number of animals

It is clear from Table 2 that when samples (1)-(9), that is, the substances or essential oils of the present invention, are applied, the hair growth is faster, for samples (1)-(4) and (8)-(9) in particular, compared to that on the nonapplication site on the control side and the site with only ethanol solution applied. From the results, it was found that the substances and the essential oils of the present invention could promote hair growth and are extremely good hair growth promoting agents.

Application Example (2): Hair lotion

(Formula)	(wt%)
(1) Camphor	0.05
(2) Hot pepper extract	0.1
(3) l-Menthol	0.1
(4) Vitamin E acetate	0.05
(5) Pulegone	1.5
(6) Denatured ethanol	60.0
(7) Fragrance	suitable amount
(8) Purified water	balance

Application Example (3): Hair cream

(Formula)	(wt%)
(1) Stearic acid	0.5
(2) Squalane	1.0
(3) Liquid paraffin	40.0
(4) Polyoxyethylene cetyl ether (20 E.O.)	1.5
(5) Polyoxyethylene cetyl ether (5 E.O.)	2.5
(6) Sorbitan monostearate	1.5
(7) Methyl paraben	0.1
(8) Triethanolamine	1.0



(9) 1,3-Butylene glycol	5.0
(10) Piperitenone	1.0
(11) Fragrance	suitable amount
(12) Purified water	suitable amount

Application Example (4): Hair shampoo

(Formula)	(wt%)
(1) Sodium alkyl ether sulfate	16.0
(2) Lauryl diethanolamide	4.0
(3) Propylene glycol	2.0
(4) Preservative	suitable amount
(5) Color	suitable amount
(6) Fragrance	suitable amount
(7) Pennyroyal oil	1.0
(8) Purified water	balance

The products of Application Examples (2)-(4) were produced by normal methods.

**Effect of the invention**

As described above, according to the present invention, substances having specific  $\alpha,\beta$ -unsaturated keto structure or essential oils containing said substances as the main components can demonstrate hair growth promoting effect. By incorporating these materials, extremely excellent hair growth promoting materials can be obtained and possibly provided for stimulating and normalizing the scalp and hair functions to give hair growth promoting and hair nourishing effects, while having high safety.

**This Page is Inserted by IFW Indexing and Scanning  
Operations and is not part of the Official Record**

**BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ **BLACK BORDERS**
- ☐ **IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- ☐ **FADED TEXT OR DRAWING**
- ☐ **BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- ☐ **SKEWED/SLANTED IMAGES**
- ☐ **COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- ☐ **GRAY SCALE DOCUMENTS**
- ☐ **LINES OR MARKS ON ORIGINAL DOCUMENT**
- ☐ **REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- ☐ **OTHER:** \_\_\_\_\_

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.**